# Laser Sintered Resorbable PCL Splints for Treating Tracheobronchalmalacia (TBM)

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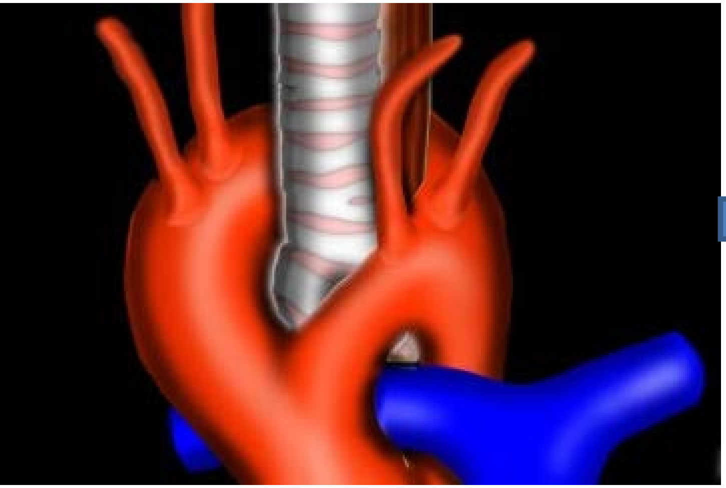
# Outline

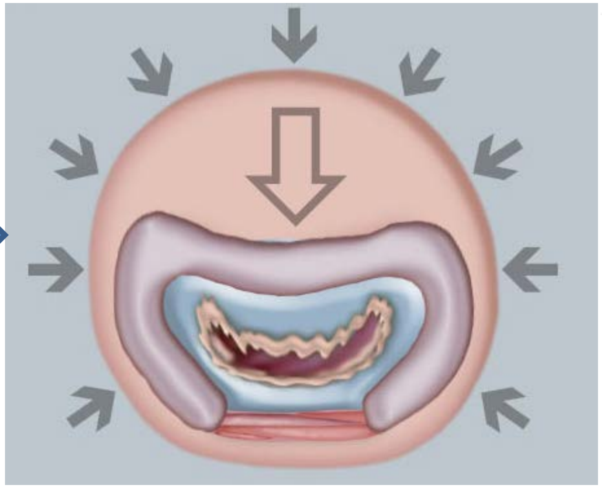
- Tracheobronchalmalacia
- Tracheal Splint Clinical Goals & Design
- Laser Sintering PCL Splints
- Clinical Use and Outcomes
- Quality Control: Current & Future

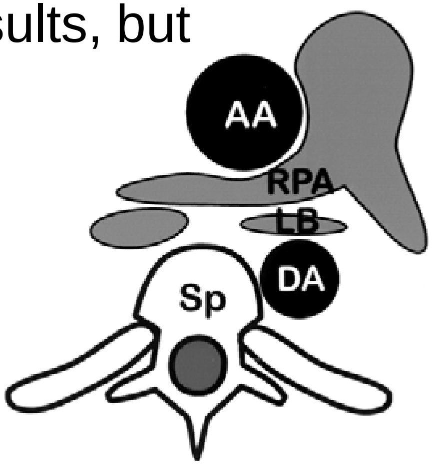
# Tracheobronchalmalacia (TBM)

# Tracheobronchalmalacia (TBM) in Humans

- Compression of airway, typically by malformed vascular structures
- Complete collapse on expiration
- Currently treated by tracheostomy/ventilators 1-2 years
- Significant complications, including death
- Need for patient specific implants due to different defect geometry (length, diameter, number)
- Stents have failed in children; FDA warning metallic tracheal stents
- Implanted splints external to airway found to give better results, but produced in an ad hoc manner






1st Patient Etiology

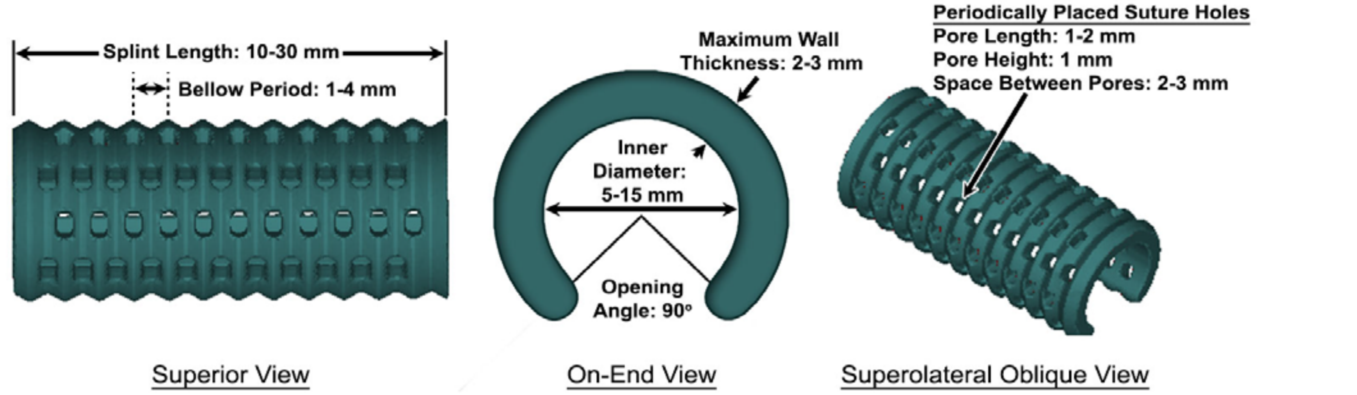
# Tracheal Splint Clinical Goals and Design

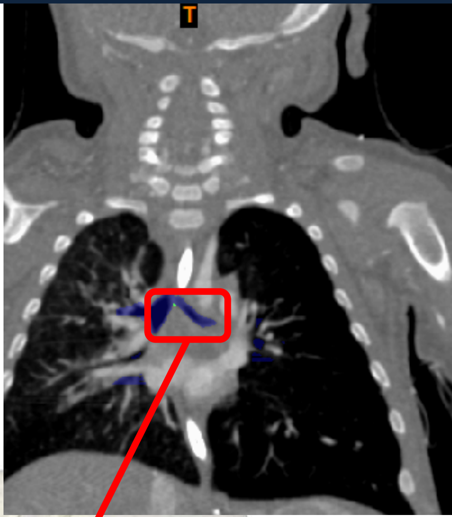
# Clinical Design Goals: Implanted Splint External to Airway

Mechanical Requirement: **M**; Biomaterial Requirement: **B**; Surgical Requirement:: **S**

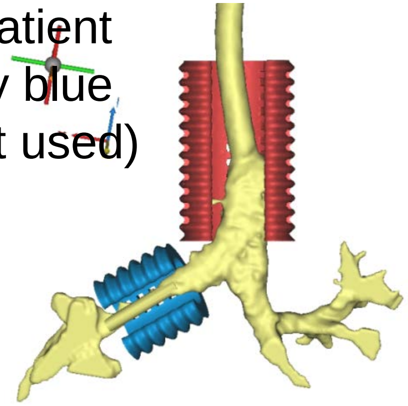
- The splint should provide radial compressive mechanical support to keep the airway open and patent: **M/B** – 0.12 MPa artery; .01 MPa exhalation
- The splint should provide this radial mechanical support for a period of 24-30 months to allow tracheal remodeling and development: **M/B**
- The splint should allow transverse and bending displacement, not interfering with cervical motion: **M**
- The splint should allow growth and expansion of the tracheobronchial complex during this 24-30 month period: M - estimated 15N growth force
- The splint should not cause adverse tissue reaction or remodeling: **B/M** - Biocompatible
- The splint should not interfere with the mucociliary architecture with the trachealbronchial lumen; it therefore should be placed externally: **B/S**
- Second surgical procedure should be avoided to remove the splint; therefore, the splint should be bioresorbable: **S/M** – resorbable in 3 years
  Surgical placement of the splint and attachment of the tracheobronchus into the splint should be straightforward: **S**; suture holes in splint to “sling” airway
- Patient Specific to account for different malacic airway diameter/length: **S/M**

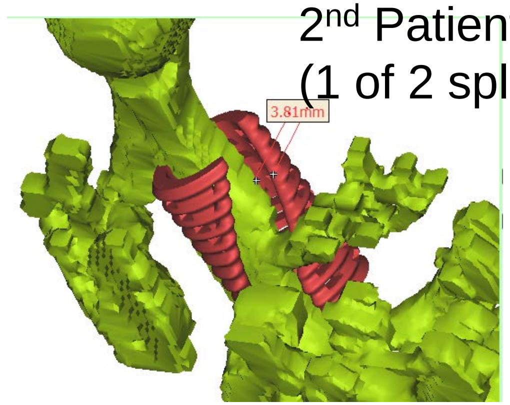
# Patient Specific Image-Based Design for Splint



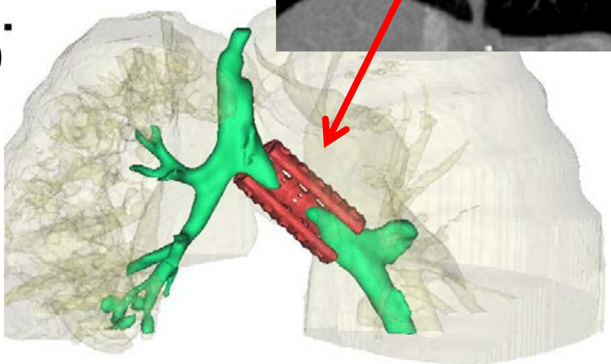




3rd Patient (Only blue splint used)





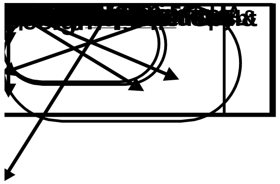

2nd Patient (1 of 2 splints)



- MATLAB program to automatically generate bellow design w suture holes
- <u>Design variables</u>: inner diameter, open angle, spiral angle , bellow height, wall thickness, suture hole width, etc (> 3,000,000 design perturbations)
- Input parameters from CT measurements from MIMICS Digital Model
- Fit splint to patient model in MIMICS
- Perform finite element analysis: compression, bending, opening (growth)
- Complex patient specific design requires 3D printing

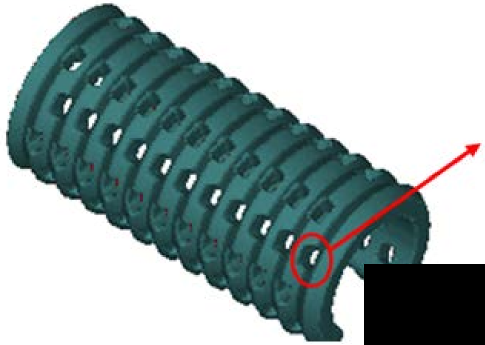
# Laser Sintering PCL Splints

# Design and Manufacture Process: Outline



# Scaffold/Implant Manufacturing by 3D Printing

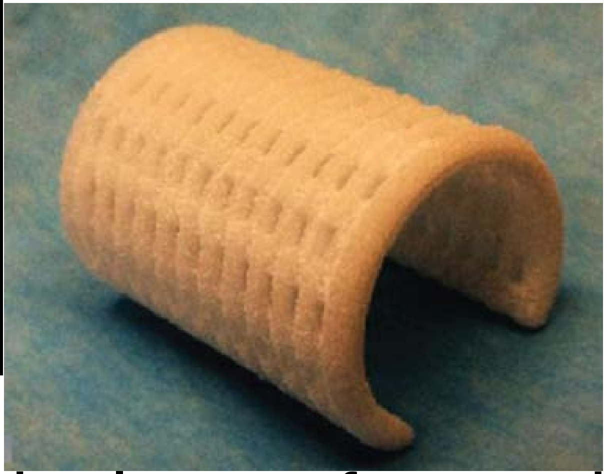
- Modular Image-Designed Scaffolds fabricated by laser sintering



Complete Video at
http://www.mottchildren.org/news/archive/201403/babys-life-saved-after-3d-printed-devices-were-implanted-u

Modular Image-Designed Scaffold

PCL Laser Sintering



Final Manufactured Scaffold

# Materials and Equipment

- EOS P100 Laser Sintering System (www.eos.info/en)
- CAPA 6501 Polycaprolactone (PCL) purchased from Polysciences (www.polysciences.com) **Target Mw = 50kDa**
- Hydroxyapatite (HA) Plasma Biotal (www.plasma-biotal.com)
- Need to Cryogenically Mill Resorbable Polymers (PCL, PLA)
  Jet Pulverizer (www.jetpulverizer.com); Fraunhofer (http://www.umsicht.fraunhofer.de/en.html) ; Evonik (http://north-america.evonik.com); Target Particle Size Range: 25μm < x < 125 μm; Median 40-60 μm

**References:**


Partee et al., 2006, J Man Sci Eng, 128:531-540
Williams et al., 2005, Biomaterials, 26:4817-4827
Eshraghi, Das, 2010, Acta Biomaterialia; 6: 2467-2476
Eshraghi, Das, 2012, Acta Biomaterialia; 8: 3138-3143
Lohfield et al., 2012, Acta Biomaterialia; 8:3446-3456
Eosoly et al., 2010, Acta Biomaterialia; 6:2511-2517

# PCL Laser Sintering Parameters

- Important PCL Laser Sintering Parameters: Bed Temperature, Laser Power, Laser Scanning Speed, Scan Spacing, Hatch Spacing, Beam Offset
  Our parameters established at University of Michigan: Partee, Hollister, Das. (2006) J Mfg Sci Eng, 128:531-540

- Laser Power: 1 - 5.4 Watts; Typically 4 Watts (UM)

- Bed Temperature: 38 – 56$^{o}$C; Typically 50-56$^{o}$C (UM)

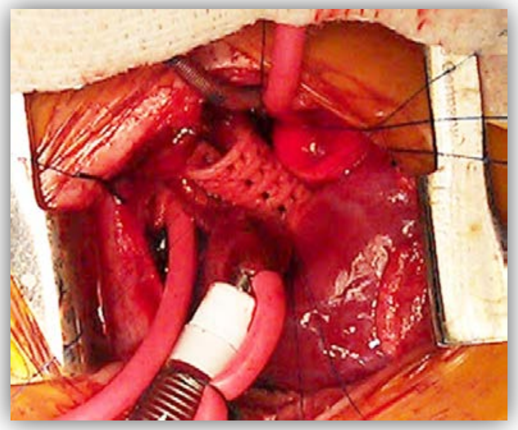
- Laser Scanning Speed: 900 – 1800 mm/s; Typically 1000-1500mm/s (UM)

- Scan Spacing: .07 - .2mm; Typically 0.15 – 0.2mm (UM)

References (see prev slide): Eshragi/Das (2010/2012); Lohfield (2012); Eosoly (2010; 2012); Partee (2006); Williams (2005)

# Clinical Use and Outcomes

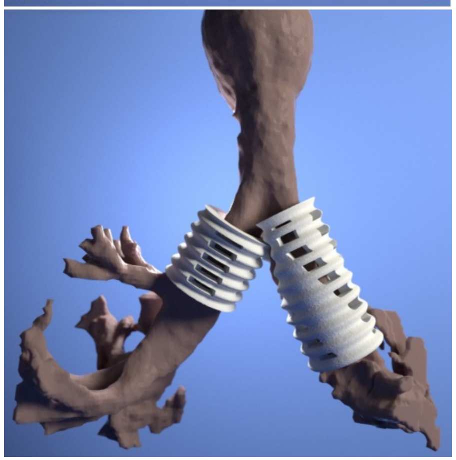
# Design & Implantation of Patient Specific Splints

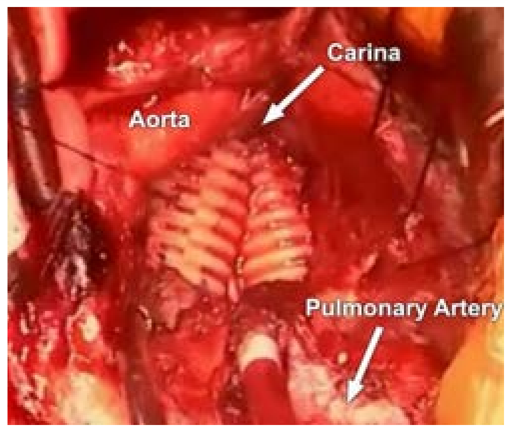


Patient 1:

Left Bronchus;

IRB Approval,
Emergency through FDA
NEJM (2013), 368:2043-2045.
31 months post-surgery

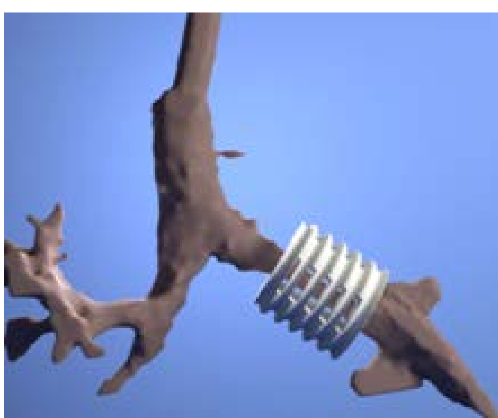


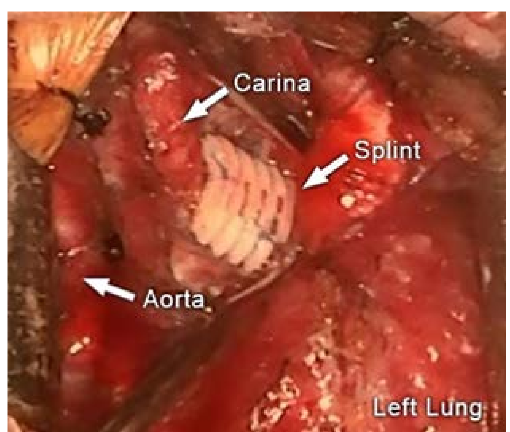



Patient 2:

Bilaterial Bronchi;

IRB Approval,
Emergency through FDA
8 months post-surgery





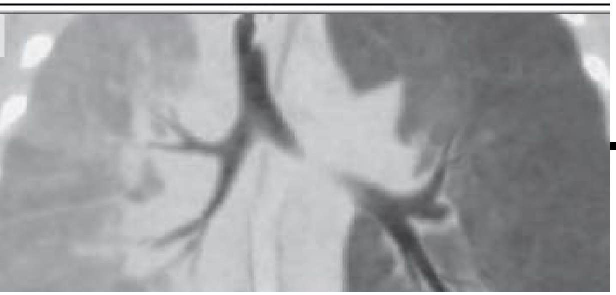

Patient 3:

Left Bronchus;

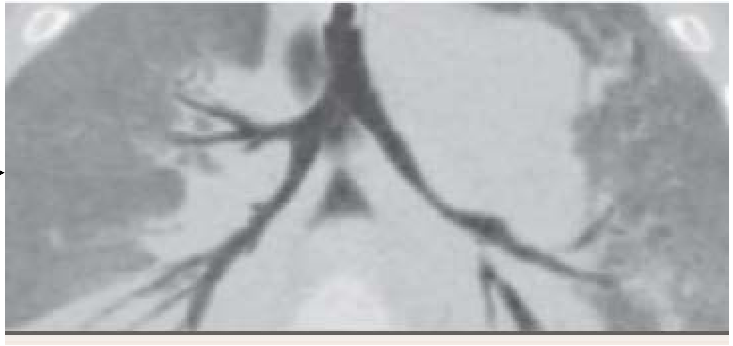
IRB Approval,
Emergency through FDA
6 months post-surgery

# Pre-Op and Post-OP Patency

**Pre-Op**



**Post-Op**

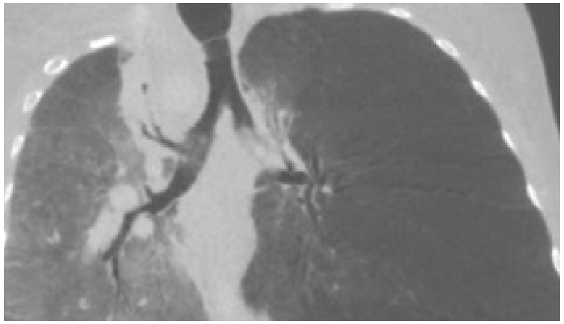


Patient 1:

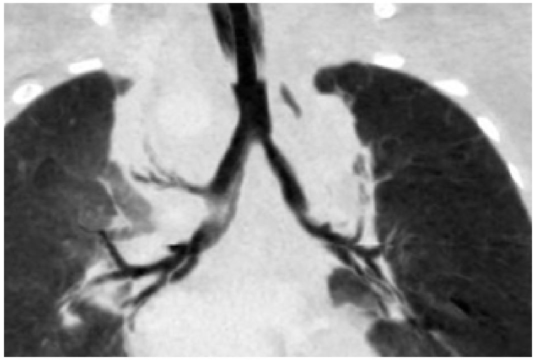
Left Bronchus;

Exhalation Scans

**Pre-Op**



**Post-Op**

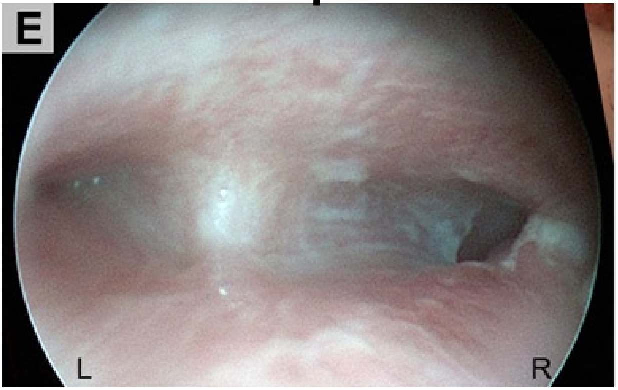


Patient 2:

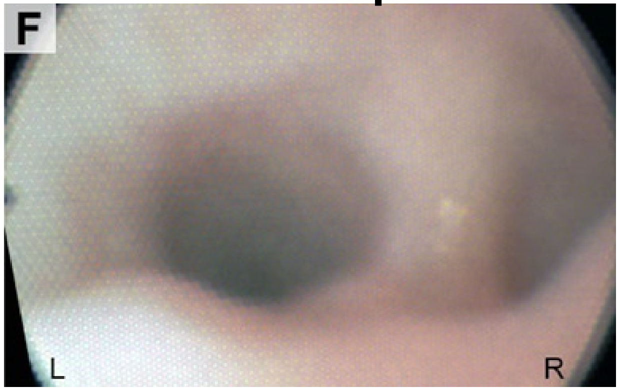
Bilaterial Bronchi;

Exhalation Scans

**Pre-Op**



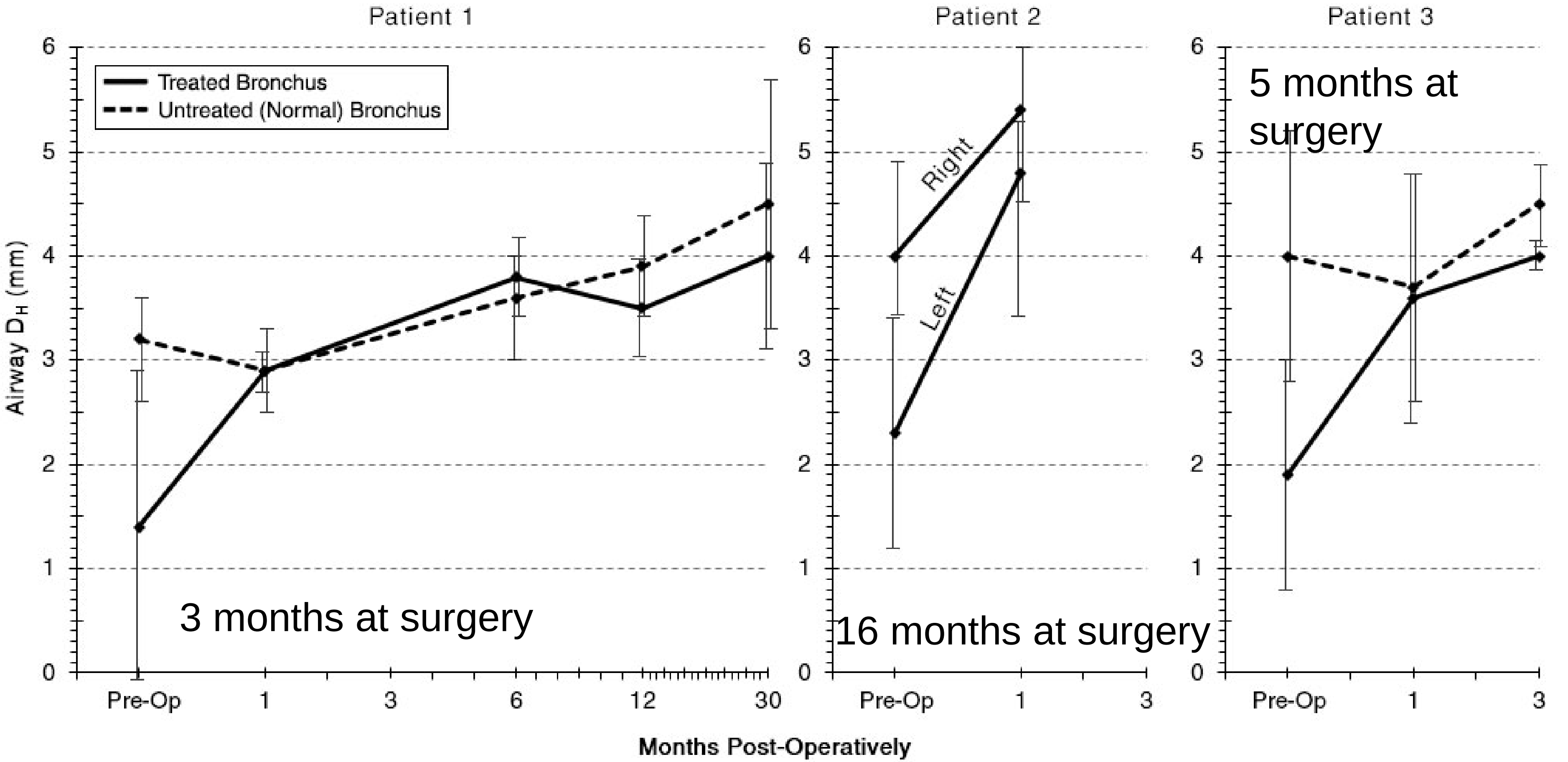

**Post-Op**



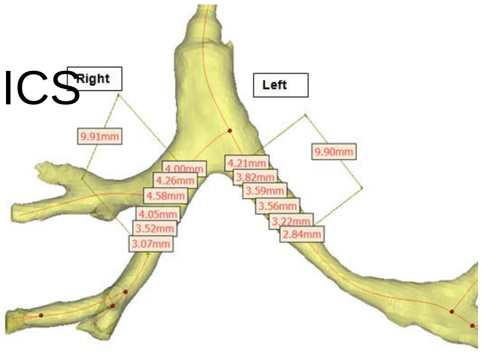

Patient 3:

Bronchoscopy

# Bronchial Growth in Patients




Hydraulic Diameter Measures Averaged along Bronchus in MIMICS



# All Patients Pre- and Post-Op

**Patient 1 – Pre-Op**

**Patient 1 – 2nd Birthday**


**Patient 2 – Pre-op 16 months**


**Patient 2 – First time sitting up**

**Patient 3 – Pre-Op**



**Patient 3 – Post-Op 2 months**

# Quality Control: Current & Future

# Quality Control Checks for Each Build

- Powder:  Check particle size range; Powder Visual Inspection; Humidity Solid Hygrometer Should be 10% to 35% relative humidity

- Build:  Check for errors on build log; visual inspection for part dragging; visual inspection for sintered “islands” when unpack build; stair stepping on parts

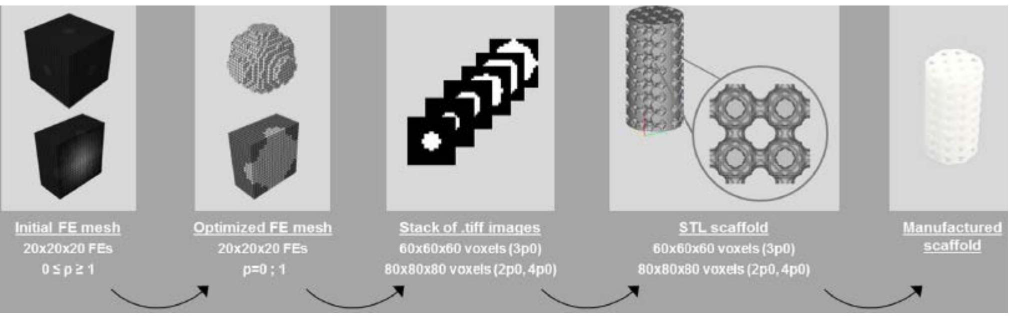
- Geometry: Caliper Measures (current); Micro-CT to assess part geometry/density (implementing)

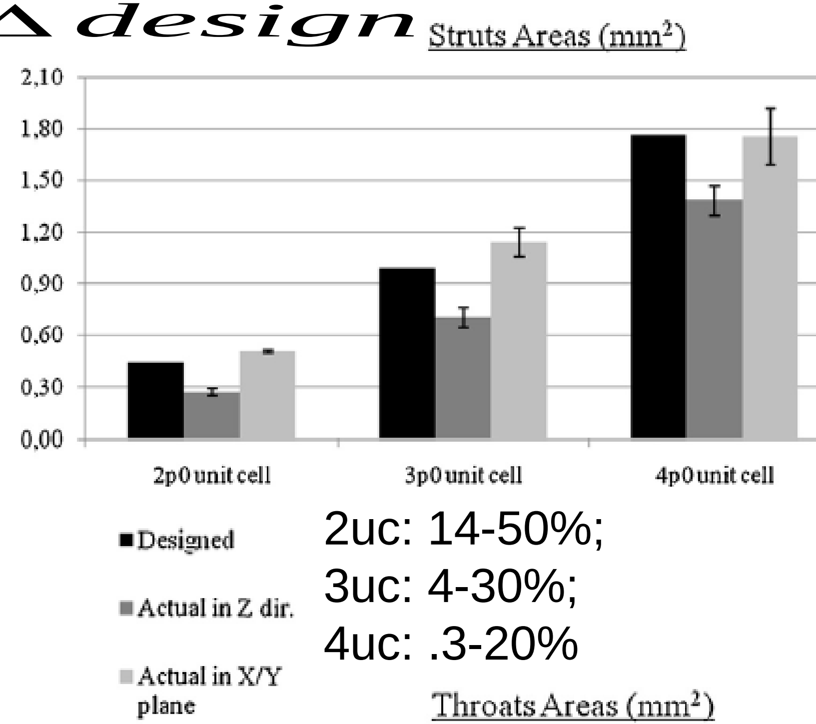
- Mechanical Properties: Standard cylindrical test specimens for modulus; splint specimens opening, compression, bending geometric stiffness (implementing)

# Geometry Quality Control

- For topology optimized (optimized for stiffness/permeability) microstructures, compare designed vs manufactured geometry by microCT (implementing for splint)

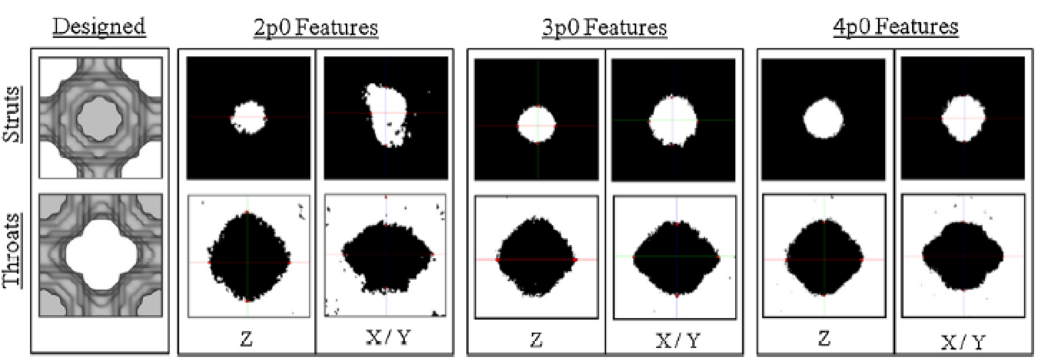
Design/Fabrication Process

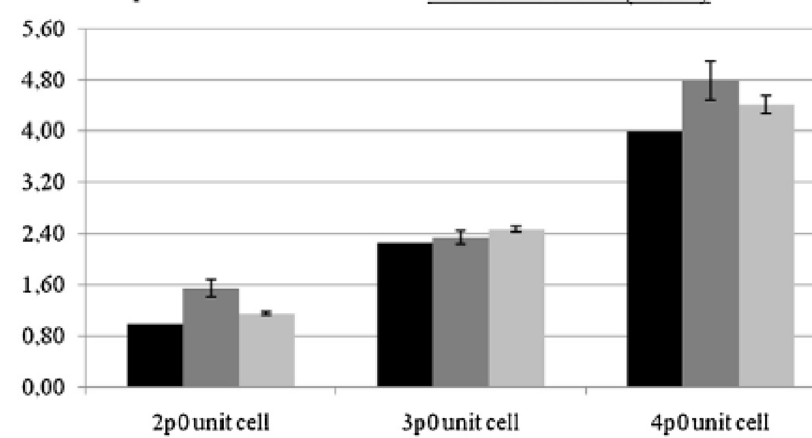



Design to Fabricated Strut/Throat Comparison

2uc: 14-50%;
3uc: 4-30%;
4uc: .3-20%



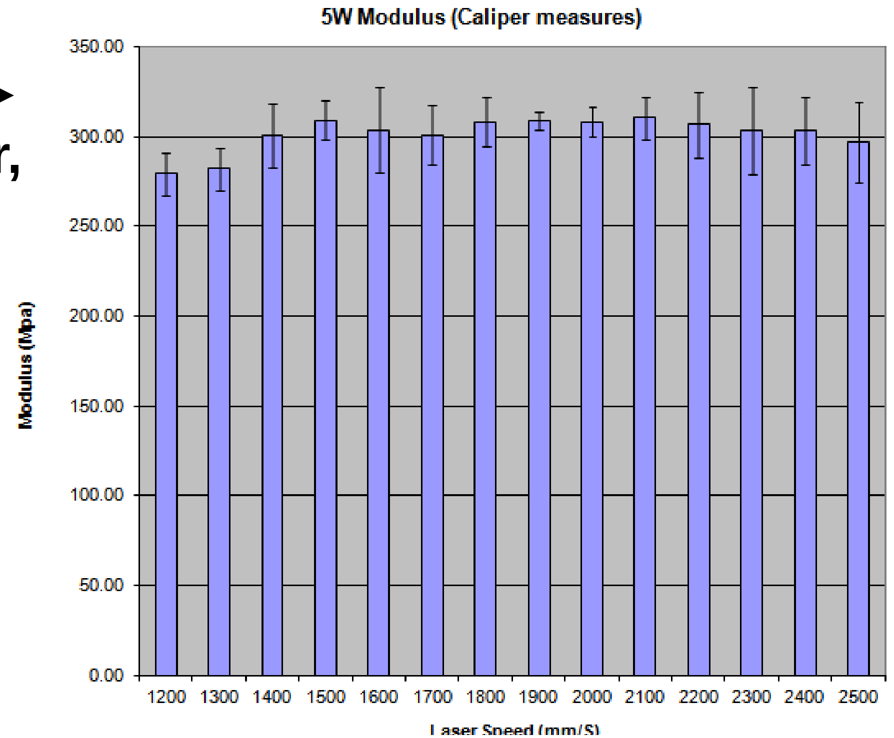

Fidelity depends on Unit Cell Size & thus Feature resolution; Dias et al, (2014), 36:448-457

# Mechanical Testing Quality Control - General

## Solid Test Cylinder Modulus

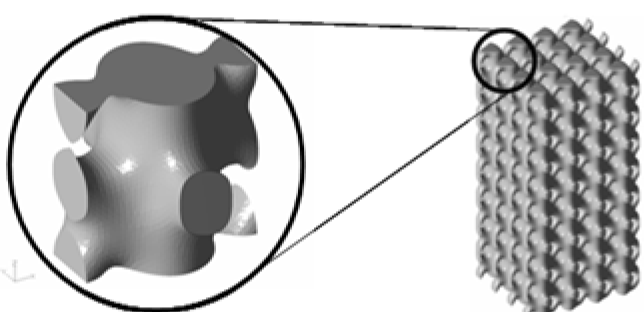
1. Affected by Laser scanning parameters: Bed Temp, Laser Power, Scan Speed 1200-2500 mm/s
2. Anisotropic due to layering

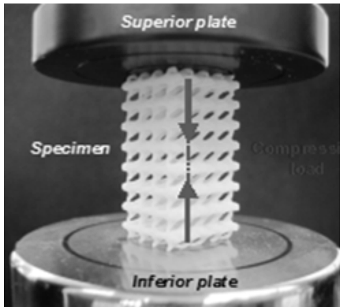
Ex = 295.5 ± 4.4 MPa parallel to bed
Ey = 292.7 ± 9.9 MPa parallel to bed
Ez = 311.7 ± 1.2 Mpa laser direction

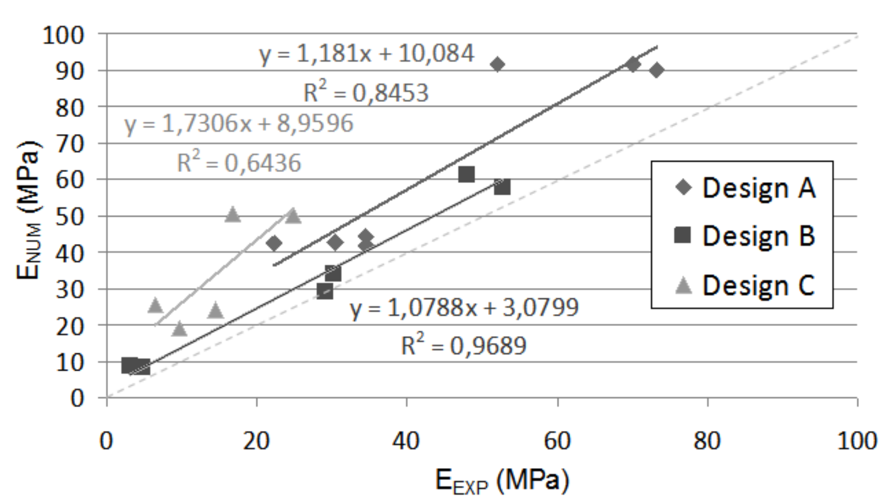



## Optimized Microstructures

1. Topology optimized for desired stiffness/permeability
2. Compare FE idealized to laser sintered mechanically tested
3. Correlation deviates from 1 to 1 as feature sizes get smaller (< 0.8mm)



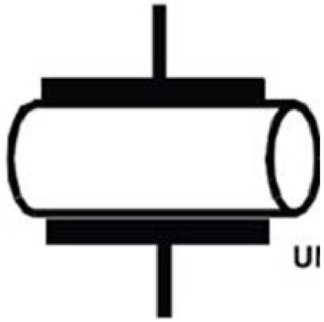



Coelho et al, (in press) Med Eng Phys

# Mechanical Testing Quality Control - Splint

**Compression:**
**Simulate exhalation loading**




**Opening:**
**Simulate growth and inhalation loading**

**Design Target:**

1. **Withstand arterial compression & respiration pressure**
2. **Allow growth**

$$Ku = f; \Rightarrow$$

$$K = \frac{f\,(artery\,/\,exhalation\ pressure * length * 1mm; \frac{N}{mm^2} * mm * mm)}{u(\mathrm{target}\langle .1comp; .2open\rangle * inner\ diameter; mm)}$$

$$Stiffness\ in\ compression\ (.12N * length\,/\,.1 * ID) > \approx 10N\,/\,mm$$

$$Stiffness\ in\ opening\ (.12N * length\,/\,.2 * OpenAngle) \leq \approx 2N\,/\,mm$$

**Patient 1 -** **Compression: 128.6 ± 11.8 N/mm; Opening: 2.77 ± 0.26 N/mm;**

**Patient 2 -** **Compression: 72.2 ± 14.6 N/mm (11mm); Opening: 1.43 ± 0.12 N/mm;**
**195.8 ± 16.2 N/mm (23mm); Opening: 2.43 ± 0.15 N/mm;**

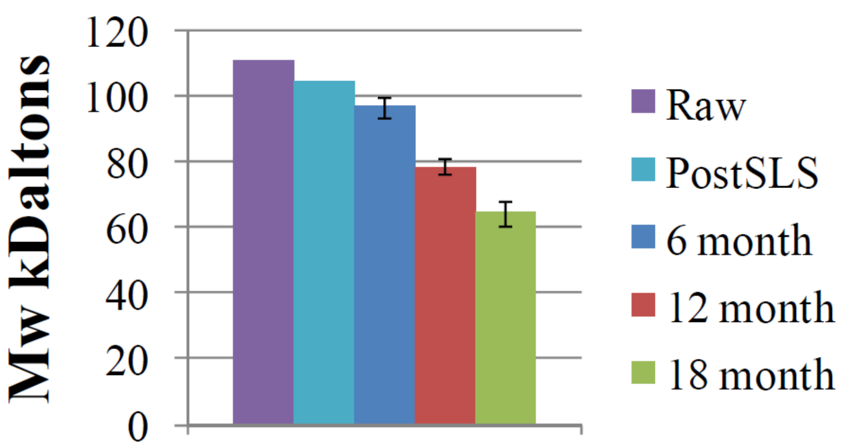
**Pig Preclinical: Compression: 28.5 ± 1.6 N/mm; Opening: .43 ± 0.05 N/mm;**
**20% growth over 8 months**

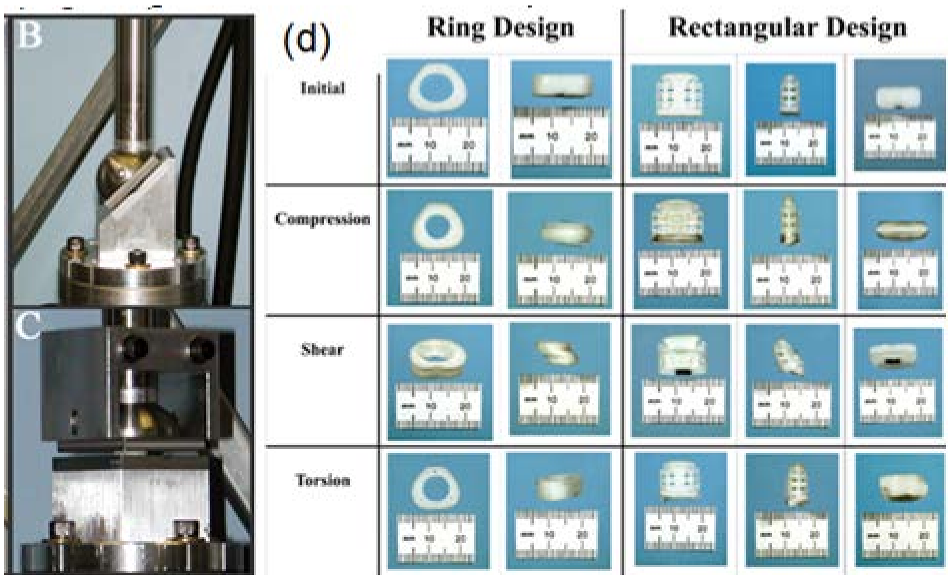
# Fatigue & Degradation Quality Control

- For resorbable materials, need to determine affect of sintering on fatigue & degradation

- Sintering doesn’t significantly change/degrade PCL molecular weight prior to implantation; ~40% loss of Mw by 18 months *in vivo* (spine cage in pig).

- Fatigue properties depend significantly on geometry; Have run spine cages to 5 million cycles in dry environment – need to test in solution



# Conclusions

- Developed Laser Sintered, resorbable PCL patient specific splint for treating tracheobronchalmalacia; Successful in 3 patients up to 31 months

- Fabricated topology optimized scaffolds with complex microstructure

- Splints with 0.4 to 2.8 N/mm opening stiffness allowed growth in patients and preclinical pig model; 28 to 195 N/mm compression stiffness protects malacic airway

- Laser parameters (scan speed, bed temp, scan power, particle size) significantly affect device geometry, mechanical properties (stiffness, strength, fatigue) & degradation (need to be tested)

- Ability to meet geometric and mechanical requirements depends on how close feature size is to minimum resolvable sintering feature -> closer to minimum feature size will mean larger deviation between design & actual properties

# Acknowledgments

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- David Zopf, MD; Robert Morrison, MD; tracheal splint
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- Chia-Ying Lin, PhD cervical spine fusion
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  ADSC
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